P10-06. Adaptive Immune Responses Elicited by Recombinant Adenovirus Vectors Exhibit Partial MyD88 Dependence

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Poster presentation

P10-06. Adaptive immune responses elicited by recombinant adenovirus vectors exhibit partial MyD88 dependence

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Background

Recombinant adenovirus (rAd) vectors elicit robust adaptive immunity, presumably as a result of efficient triggering of innate immune pathways. Here, we examined the contribution of Toll-like receptor (TLR) signaling to shaping antigen-specific CD8+ T-cell responses generated by rAd vectors in mice.

Methods

C57BL/6 (WT), MyD88-/-, TRIF-/- and TLR9-/- mice were immunized with a single i.m. injection of rAd5, rAd5HVR48, rAd26 or rAd35 expressing SIV-Gag. Following immunization, Gag-specific cellular immune responses were assessed by D^b/AL11 tetramer binding assays and IFN-gamma ELISPOT responses.

Results

MyD88-/- mice immunized with 3×10^8 vp of each respective rAd vector generated significantly diminished tetramer-positive CD8+T-cell responses as compared with WT mice. By day 28 post-immunization, rAd5-Gag produced mean tetramer-positive responses of 3.5% in MyD88-/- mice as compared with 12.6% in WT mice ($p = .0004$). Similarly, tetramer-positive responses elicited by rAd5HVR48-Gag (4.4% vs 9.0%), rAd26-Gag (0.3% vs 6.3%) and rAd35-Gag (3.7% vs 6.6%) were also significantly diminished in MyD88-/- mice as compared with WT mice. These results were confirmed by functional IFN-gamma ELISPOT assays. However, dependence on MyD88 was overcome when rAd vectors were given at higher doses. In contrast, TRIF-/- mice immunized with 3×10^8 vp of rAd vectors mounted comparable or higher tetramer-positive responses as compared with WT mice. TLR9-/- mice immunized with these rAd vectors displayed no difference in antigen-specific CD8+ T-cell responses when compared to WT mice.

Conclusion

These data show that antigen-specific CD8+ T-cell responses elicited by rAd vectors are diminished in the absence of MyD88 signaling. The absence of TRIF did not impair the immunogenicity of rAd vectors. The partial dependence on MyD88 could be overcome by increasing vector dose, suggesting that both MyD88-dependent and -independent pathways contribute to adaptive immune responses elicited by rAd vectors.